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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,120	04/12/2006	Moller Peter Hundahl Niels	6581.204-US	4545

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
04/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/531,120	NIELS ET AL.	
	Examiner	Art Unit	
	FOZIA M. HAMUD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/13/2005; 10/17/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed on 11 April 2005 is acknowledged. Claims 1-13 have been cancelled and new claims 14-33 have been added. Thus claims 14-33 are pending and under consideration. No new matter has been introduced.

Specification:

2a. The amendment to the specification filed on 11 April 2005, correcting priority information is acknowledged. No new matter has been introduced.

2b. The status of the international parent Application PCT/DK2003/000691, must be corrected, by inserting WO 2004/032953 after the filing date of said application.

Sequence Compliance

3a. The sequences have been received on 20 February 2008 and comply with the requirements of 37 CFR §1.821 through §1.825.

3b. Sequences are disclosed in table A on page 17, however, these sequences are not accompanied by the required reference to the relevant sequence identifiers, as required by 37 CFR §1.821 through §1.825. Appropriate correction is required.

Priority:

4. Based on the information given by Applicants and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in this application is supported by parent Provisional Application Number: 60/419,225, filed on 17 October 2002. Accordingly, the subject matter defined in claims 14-33 is afforded an effective filing date of 17 October 2002.

Information Disclosure Statement:

5. The information disclosure statement (IDS) submitted on 17 February 2006 has been received and complies with the provisions of 37 CFR §1.97 and §1.98. The references in the parent application number 10/06,106 have been considered as to the merits.

Claim rejections-35 USC § 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claims 14-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

The instant claims encompasses a method of treating an allergic condition in a patient or a method of treating a parasitic disease in a patient or a method of inducing a protective eosinophil-mediated response in a patient, said method comprising administering an effective amount of IL-21 to the patient, or administering a polypeptide that is 70%, 80% or 90% identical to the polypeptide of SEQ ID NO:2.

The instant specification discloses IL-21 mRNA is expressed in Hodgkins lymphoma with easinophil infiltration, (see figure 1a) and that IL-21 mRNA is also diffusely expressed in lymphocytes in both the easinophilic and lymphocytic types of histopathology, (see figure 3). The specification contemplates that the expression of IL-21 in eosinophils may indicate that said eosinophilic IL-21 exerts a protective role and

that eosinophilic infiltration or increased number of eosinophils in body fluids and/or tissues in certain disorders or disease states or conditions may indicate that said eosinophils play a protective role by releasing IL-21, which in turn reduces an allergic reaction or allergic disease, (see page 14, lines 8-20). Thus, the specification speculates that the administration of IL-21 may be useful in the treatment of allergic diseases, such as asthma, or in the treatment of parasitic disease. However, the specification does not disclose a method of treating any patient by administering IL-21.

Furthermore, the state of the art acknowledges that IL-21 exerts pleiotrophic immunomodulatory activities on a variety of target cells including B, T and NK cells that undergo class switch recombination. Specifically, there have been contradictory reports as to whether IL-21 suppresses or enhances IgE, (the immunoglobulin isotype that plays a pivotal role in the pathogenesis of many allergic diseases, such as asthma). For example, Suto et al, (cited on the IDS filed on 06/13/2005) teach that the in vivo injection of 1L-21 prevented antigen specific IgE production on immunization (Figure 1) and that IL-2 l inhibited IL-4-induced germ line Cε transcription in B cells (Figure 5). However, Suto et al state that whereas IL-21 strongly inhibited LPS/IL-4-induced IgE production in vitro, the effect of IL-21 on antigen-specific IgE production in-vivo was modest. Suto et al also teach that when unfractionated splenocytes instead of purified splenic B cells were used as a source of B cells, much higher concentrations of IL-21 were required to achieve comparable inhibitions of LPS/IL-4-induced IgE production, (see page 4572, column 2). Novak et al (WO 00/53761, September 2000) disclose IL-21 polypeptide and nucleic acid encoding it, (see claims and SEQ ID NO:2). However,

Novak et al do not teach a method of treating allergic condition using said IL-21. It has also been reported that mice genetically deficient for IL-21R or IL-21 exhibited more abundant production of IgE than did wild type mice in response to immunization with antigens, (see Ozaki et al Science, 298, November 2002, pages 1630-1634, especially page 1632) and Shang et al, Cellular Immunology, Vol. 241, July 2006, pages 66-74, especially abstract and page 73). However, another report demonstrated that IL-21 enhanced production of IgE by unfractionated peripheral blood mononuclear cells (PBMC) or B cells cultured in the presence of anti-CD40 and either IL-4 or IL-13, whereas IL-21 interfered with the IgE production by PBMC stimulated by PHA and IL-4, (see Wood et al, Cellular Immunology, 2004, Vol. 231, pages 133-145, especially see pages 137 and 138). Wood et al conclude that IL-21 either stimulates or inhibits IgE production depending on activation conditions, (see page 143, column 1). Caven et al also show that IL-21 elevated IgE production and proliferation of B cells when the cytokine was added to PBMC or tonsilar B cells stimulated by anti-CD40 and IL- 4, (see Caven et al, Cellular Immunology, 2005, Vol. 238, pages 123-134). Caven et al demonstrate that IL-21 can cause both enhancement and inhibition of IgE in both human and mouse in-vitro systems, depending upon the cell density examined, (see abstract and page 133, column 2). Finally, Pene et al show that IL-21 differentially regulates IL-4-induced human IgE production depending on the genotype of the IL-21R gene (Journal of Immunology, Vol. 177, 2006, pages 5006-5013), Thus, there have been contradictory reports as to whether IL-21 suppresses or enhances IgE and the instant specification fails to add anything to clarify this inconsistency.

The specification also fails to establish a link between IL-21 and "a parasitic disease". Finally, the specification is not enabling for "inducing a protective eosinophil mediated response in a patient", because it fails to identify said patient, or which diseases should the patient be protected from. The fact that IL-21 mRNA is expressed in Hodgkins lymphoma with easinophil infiltration, does not enable the claimed method, because the specification does not show that said expression leads to protect any patient from any disease.

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, all that is disclosed in the specification is that IL-21 mRNA is expressed in Hodgkins lymphoma with eosinophil infiltration. The specification speculates that eosinophils play a protective role by releasing IL-21, which in turn reduces an allergic reaction or allergic diseases, however, there is no disclosure that IL-21 is actually used in any treatment or any in-vitro or in-vivo model, nor is there any guidance in the specification as to an amount of IL-21 that is sufficient to effect any treatment. Therefore, due to the lack of guidance in the specification, the complex nature of the invention coupled with the state of the prior art, which discloses contradictory reports as to whether IL-21 suppresses or

enhances IgE, (the immunoglobulin isotype that plays an important role in the pathogenesis of allergic disorders, such as allergic asthma, allergic rhinitis, and atopic dermatitis), the claimed invention is rendered nonenabling.

5b. Claims 20-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 20-33 encompass a method of administering an IL-21 polypeptide comprising an amino acid sequence that is at least 70%, 80% or 90% identical to the polypeptide of SEQ ID NO:2. However, the claims do not require that the polypeptide to be administered in the claimed method possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims encompass administration of a genus of polypeptides that is defined only by sequence identity.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing

identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the IL-21 comprising the amino acid sequence set forth in SEQ ID NO:2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that

the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115)

Conclusion:

6. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FOZIA M. HAMUD whose telephone number is (571)272-0884. The examiner can normally be reached on Monday-Friday: 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
20 March 2008

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646